AN EVALUATION OF ANGIOGRAPHY, ^{75}Se-METHIONINE SCINTIGRAPHY AND THE LUNDH TEST IN THE DIAGNOSIS OF PANCREATIC DISEASE.

by

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Abstract

In order to assess accuracy and consistency of diagnostic opinion in suspected pancreatic disease, using available diagnostic procedures, 74 patients, subjected to selective angiography, pancreatic function test (Lundh test), and scintigraphy, were studied retrospectively. The patients were divided into four diagnostic subgroups, three of which represented defined pancreatic disease, the fourth serving as a control group since such disease could be excluded.

The primary diagnostic results were compared. After a stipulated minimum of six months the angiographic films and scintigraphic recordings were re-appraised in a randomized manner without access to clinical data. The evaluations thus achieved were compared to those delivered primarily.

The results of the present study seem to indicate that the Lundh test and pancreatic scintigraphy are screening tests with a high level of diagnostic reliability and consistency; when normal, practically ruling out pancreatic disease. Angiography is recommendable only if one or both of the above mentioned screening methods yield pathologic results, supported by clinical evidence. The principal aims of selective angiography in suspected pancreatic disease, are to map vascular anatomy, to differentiate non-neoplastic disease from cancer and to assist estimation of operability. The results of the re-appraisal indicate that the diagnostic accuracy of angiography, more than that of scintigraphy, is dependent on the experience of the examiner.

Verification of diagnosis in suspected pancreatic disease is often a touchstone to the clinican. To the surgeon, two conditions are of particular interest. Firstly, of course, early neoplastic disease and secondly advanced chronic pancreatitis and its sequelae, as surgical intervention has proved to bring considerable relief of the severe pains associated with this condition (Puestow & Gillesby 1958, Warren 1971, Keith & White 1973, Arnesjö et al., 1975, Frey et al., 1976, Jordan 1977).

As quite many patients are admitted to hospitals with epigastric pain or discomfort, where diagnosis is not apparent after first line procedures such as radiologic G.I. examinations and gastroscopy, it seems important to establish the accuracy of available diagnostic tools in suspected pancreatic disease. The present study aims at an objective analysis and comparison of angiography, pancreatic scintigraphy and exocrine function test (Lundh test) in order to determine the most satisfactory procedures for routine clinical use.

Material

The material comprises all of the 74 patients in whom angiography, pancreatic function test and scintigraphy were performed at the University Hospital of Lund between 1972 and 1974. The patients were divided into diagnostic subgroups:

1. Pancreatic cancer
2. Chronic relapsing pancreatitis
3. Acute relapsing pancreatitis
4. Epigastric pains

Diagnosis

All cases of pancreatic cancer and chronic relapsing pancreatitis were subjected to laparotomy and diagnosis was verified histologically and/or cytologically by fine needle aspiration biopsy.

The diagnosis of acute relapsing pancreatitis was made in patients having had 2 or 3 attacks of pancreatitis subsiding without complications. In the intervals between attacks the patients were completely free of symptoms. In none of these patients had diabetes, signs of biliary tract disease or pancreatic calcifications been evident. Fecal fat excretion was normal in all these patients.

In group 4 (epigastric pains) the final diagnosis was gastritis and/or duodenal ulcer in 13 cases, aneurysma of the splenic artery in one case, nodular hyperplasia of the liver in one case and Crohn´s disease without signs of malabsorption in one case. Nine of the 16 patients were subjected to laparotomy, at which the pancreas was found completely normal.

Methods

The angiographic examinations were performed as selective catheterization of the coeliac and superior mesenteric arteries usually with simultaneous injection of the contrast medium. Superselective catheterization of the hepatic and/or gastroduodenal artery was moreover carried out in some patients as found necessary.

Scintigraphy was performed using i.v. injection of 200 μCi ^{75}Se-methionine and 2 mCi of $^{99}Tc^{m}$-sulphur colloid simultaneously. With a gamma camera connected to a digital system, static imaging of the ^{75}Se-methionine in the liver and pancreas was started about 20 minutes after injection, followed by an image of the $^{99}Tc^{m}$-sulphur colloid in the liver. The system permitted electronic subtraction of overlapping liver tissue.

The exocrine pancreatic function was investigated after stimulation by a test meal as described by Lundh (1962). The duodenal aspirates were collected by a single lumen plastic tube with the tip at the ligament of Treitz. The tube was passed under fluoroscopic control. The aspirates were collected in 10 minute aliquots during the first hour and in 30 minute aliquots during the second hour. The aspirates were immediately frozen to -20°C, at which temperature they were stored until analyzed. From each of the eight fractions 1 ml was withdrawn, shaken for 2 minutes and pooled. Within a week the trypsin activity of the pooled fractions were determined by automatic titration using para-toluene-L-arginine methyl ester (TAME) as substrate. A trypsin level short of 37 U/ml was considered subnormal (Ihse et al. 1977).

Interpretation of angiographic and scintigraphic images.

All angiographic examinations were reviewed by a senior radiologist who had not in the majority of cases made the original reports on the findings. The re-appraisal was performed in a randomized manner without access to the patient´s name, case history or any clinical data whatsoever. The diagnostic criteria used were those previously described by Tylén 1973 and Tylén & Arnesjö 1973 (a).

A similar procedure was followed reviewing the gamma camera images. (Agnew et al. 1976).

A minimum of 6 months since the last evaluation of the angiographic and scintigraphic examination was stipulated, as in some cases the reviewer also had done the primary evaluation.

Results

1. Cancer of the pancreas (n = 24).
Falsely negative angiographic report was at hand primarily in 4 out of 24 cases and on review in 1 (Fig. 1). Thus, the diagnostic accuracy was enhanced from 20/24 (83%) on first analysis to 23/24 (96%) on review. In 1 case only was angiographic diagnosis false-negative at both occasions of evaluation. Scintigraphy was considered pathologic on both occasions of analysis in all cases. Trypsin levels were subnormal in all but two instances. Thus, in one case, scintigraphy was the only test indicating pancreatic disease, while, at least two of the examinations were positive in the remainder. Eight of the 24 patients were successfully operated upon with total pancreatectomy.

2. Chronic relapsing pancreatitis (n = 25).
The angiographic examination was primarily incorrectly interpreted as negative in 7 out of 25 cases and in 2 on re-appraisal which improved diagnostic accuracy from 18/25 (72%) to 23/25 (92%) (Fig. 2). In 1 case angiography was false-negative at both occasions of evaluation. Scintigraphy was considered normal in 1 case primarily in 2 on review. Trypsin levels were subnormal in 22 cases. In 15 cases pancreatic disease was indicated by all three procedures but it should be noted that trypsin determination was normal in 3 patients in whom both angiography and scintigraphy were pathologic. On the other hand trypsin was the only abnormal test in one patient.

3. Acute relapsing pancreatitis (n = 8).
Angiography was considered pathologic primarily in 4 cases and on second analysis in 2 of these (Fig. 3). Scintigraphy was considered pathologic on both occasions in 2 instances and on review in additionally 1. Trypsin levels were normal in all but 1 patient.

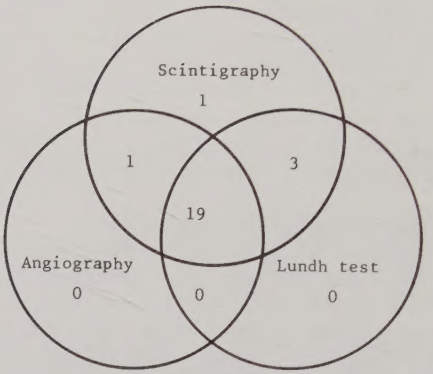
4. Epigastric pains (n = 16).
All angiographies were considered normal (Fig. 4). Scintigraphy was falsely pathologic primarily in no case, on re-appraisal in 1. Trypsin levels were normal in all cases.

Discussion

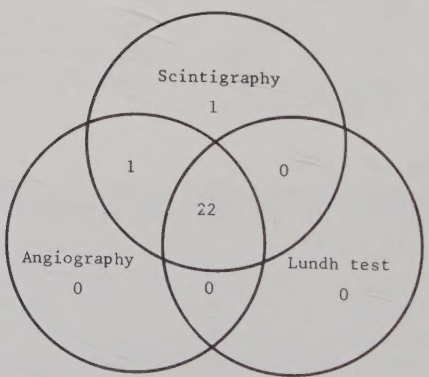
Reviewing the results of examinations "blindly", represents of course, a theoretical situation with no relation to normal practical work. The thought behind it was partly to relieve the evaluation from the bias of clinical information and partly to estimate the consistency of diagnostic opinion when passing new judgement on the findings after a relatively long period of time.

It is interesting to note that so many carcinomas were overlooked at angiography on primary analysis. On review, however, diagnostic accuracy was improved considerably, although clinical data were withheld. This

Pancreatic carcinoma (n = 24).



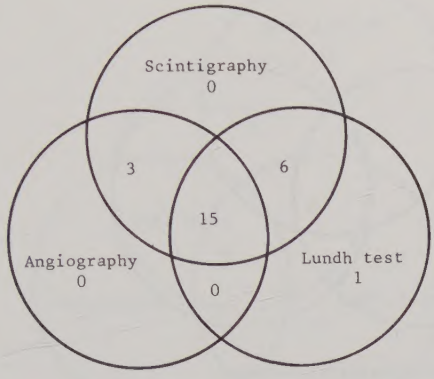
Pathologic diagnostic findings primarily.



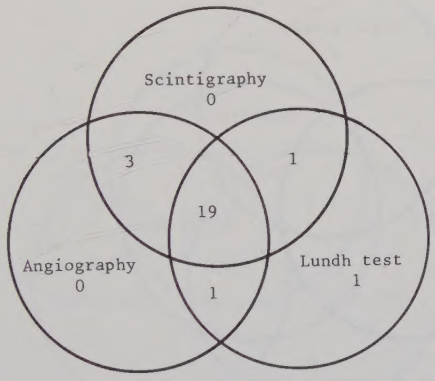
Pathologic diagnostic findings on review.

Fig. 1. Results of angiography, scintigraphy and Lundh test, primarily and on review in 24 cases of pancreatic carcinoma. The sum of the figures within each circle, represents the total number of pathologic findings with the respective diagnostic method.

Chronic relapsing pancreatitis (n = 25).



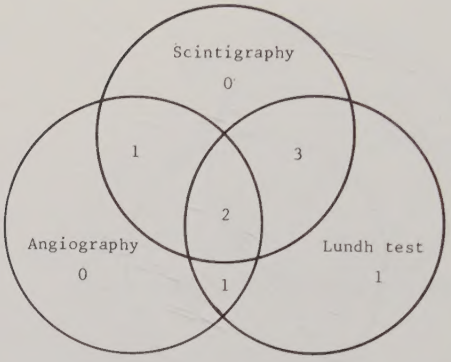
Pathologic diagnostic findings primarily.



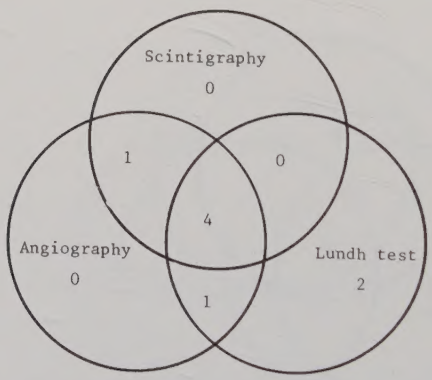
Pathologic diagnostic findings on review.

Fig. 2. Results of angiography, scintigraphy and Lundh test, primarily and on review in 25 cases of chronic relapsing pancreatitis. The sum of the figures within each circle, represents the total number of pathologic findings with the respective diagnostic method.

Acute relapsing pancreatitis (n = 8).



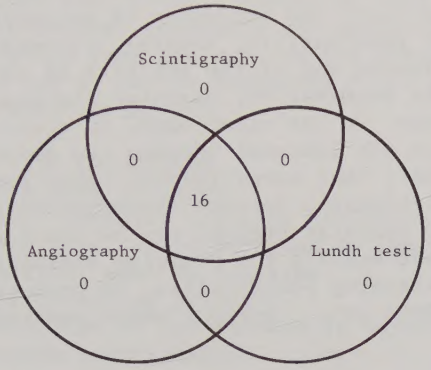
Normal diagnostic findings primarily.



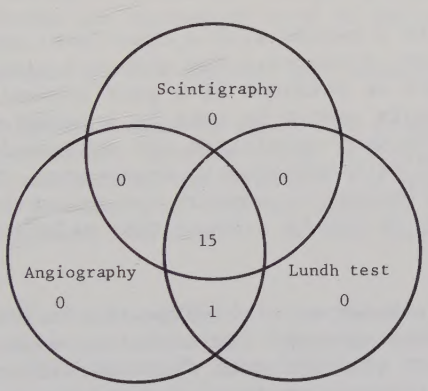
Normal diagnostic findings on review.

Fig. 3. Results of angiography, scintigraphy and Lundh test, primarily and on review in 8 cases of acute relapsing pancreatitis. The sum of the figures within each circle, represents the total number of normal findings with the respective diagnostic method.

Epigastric pains (n = 16).



Normal diagnostic findings primarily.



Normal diagnostic findings on review.

Fig. 4. Results of angiography, scintigraphy and Lundh test, primarily and on review in 16 cases of epigastric pains. The sum of the figures within each circle, represents the total number of normal findings with the respective diagnostic method.

points at the wellknown fact that the angiographic diagnosis is difficult and that experience in pancreatic angiography is needed to achieve good results (Tylén 1973).

The improvement of the diagnostic accuracy on review of the angiographic examinations of the patients with chronic relapsing pancreatitis emphasizes the same fact. The incidence of angiographic pathologic findings in chronic pancreatitis, however, is very much dependent on the duration of the disease and of the activity of the inflammatory process at the time of the examination; vascular changes increase with the duration of the disease. On the other hand, in acute relapsing pancreatitis, the gland in the interval between two attacks returns to normal. We know, however, that normalization takes some time and depending on the time relationship between the acute attack and the angiographic examination, vascular changes may be demonstrated (Tylén et Arnesjö, 1973). This may explain the positive angiographic findings in patients with acute relapsing pancreatitis. No angiographic changes were evident in the patients in group 4 where pancreatic disease was excluded.

The results suggest that the over all accuracy of angiography in pancreatic disease is high, provided that the interpretation is performed by an experienced examiner. The diagnosis of chronic pancreatitis would appear to be less accurate than that of pancreatic carcinoma.

Scintigraphy is found to be a method with a high level of diagnostic reliability and consistency, discerning the affected pancreas from the normal gland. Therefore we consider it a good screening procedure. Final, preoperative diagnosis cannot be made by scintigraphy alone since it fails to discriminate between neoplastic and inflammatory disease and to establish the extent of extra-pancreatic engagement. The falsely pathologic scintigraphic findings in some of the patients with acute relapsing pancreatitis may be due to a short time relation to the acute attack.

In one of the patients in the group with epigastric pains, the uptake of the radionuclide may have appeared diminished on account of gross obesity. This situation can also arise in diabetes, after vagotomy and gastric surgery, in cirrhosis of the liver, ascites and in starvation among other reported clinical conditions (Agnew et al. 1976).

Trypsin levels were subnormal in 22 of the 24 patients with pancreatic cancer and in 22 out of 25 patients suffering from chronic pancreatitis The fact that one of the function tests was performed only shortly after the subsidence of an attack in a patient with acute relapsing pancreatitis, may be responsible for the low trypsin level in this case.

Percutaneous transhepatic cholangiography (PTC) (Wiechel, 1964; Marions, 1974) and endoscopic retrograde cholangio-pancreatography (ERCP) (Cotton, 1972; Belohlavek et al. 1976) has been reported to be of great value in the diagnosis of pancreatic disease, especially in patients with obstructive jaundice. Experiences with ultrasound scanning are yet limited. Encouraging results have, however, recently been reported (Bruce et Pearce, 1976). Determination of pancreatic iso-amylase in serum may be a simple and reliable screening test (Skude et Ihse, 1977). Further studies are however necessary for definite evaluation of the method. The experiences from the work on the present and related studies in the field, have led us to the following order of diagnostic procedures in suspected pancreatic disease:

1. First line procedures.
   a/ Jaundiced patients.
   PTC with remaining catheter diverting the bile.
   Directed fine needle biopsies during the cholangiographic examination, when so required.
   b/ Non-jaundiced patients.
   Determination of iso-amylase in serum.
   Pancreatic scintigraphy.
   Lundh test.
   Ultrasonic scanning.

2. Second line procedures.
   ERCP.
   (This method is used to obtain details if any of the above procedures has succeeded - or failed - to localize the lesion).
   Angiography of the coeliac and superior mesenteric artery.

The results of the methods used by us in the present investigation in the diagnosis of pancreatic disease bring a fairly high accuracy used one by one and in combination the failures are exceptionally few. It should, however, be pointed out that in contrast to the Lundh test and scintigraphy, angiography can discern chronic pancreatitis from carcinoma of the pancreas.

More than two thirds of all patients with pancreatic carcinoma present with jaundice. In these patients the first procedure should be PTC offering both diagnosis (Wiechel 1964; Marions 1974) and relief of biliary stasis by establishment of percutaneous drainage (Tylén et al. 1977). The drainage period may then be used for additional investigations Screening for evidence of pancreatic disease should first be undertaken in the non-jaundiced patient. Here the Lundh test and scintigraphy may be used in the first line. If these two latter tests are normal, pancreatic disease is practically ruled out and only exceptionally strong clinical evidence may necessitate an angiography. Pathologic finding in one or both of the screening procedures makes angiography recommendable. By angiography the nature of the disease may be revealed and this may also be supported by fine needle biopsy towards the lesion

guided by the angiographic findings (Tylén et al. 1976). Provided that pancreatic carcinoma is diagnosed an evaluation of the resectability may also be made (Tylén et Arnesjö, 1973).

In conclusion, the findings of the present study seem to demonstrate pancreatic scintigraphy and the Lundh test as reliable tests. The fact that scintigraphy and Lundh test are relatively inexpensive and non-traumatic to the patient makes these tests suitable for screening purpose. The accuracy of angiographic interpretation is somewhat dependent on subjective evaluation. Thus, the experience of the examiner appears to be a critical factor, which - to a certain extent - is true also regarding scintigraphy. The value of angiography is threefold, firstly to map vascular anatomy, secondly to differentiate non-neoplastic disease from cancer and thirdly to estimate resectability.

Acknowledgement

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